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CASE REPORT

# Reversible valproate-induced choreiform movements

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Valproate is an anticonvulsive drug whose mechanism of action is based on GABAergic systems. One of the infrequent adverse effects of valproate is choreiform movements. In our study, we report a patient having head trauma history with partial and secondary generalized seizures taking 1500 mg/day valproate. During the second month of the therapy, generalized chorea was observed. Since other aetiologic causes of chorea were excluded, acutely occurring chorea in the patient was thought to be related with valproate usage because of persistence of choreiform movements for days without any fluctuation. Valproate was stopped slowly and lamotrigine was added at a dose of 400 mg/day. Within a two-month period after cessation of the valproate, choreiform movements had disappeared. We thought that the history of head trauma and another antiepileptic drug usage were the risk factors for the occurrence of valproate-induced choreiform movements.



*Key words:* valproate; chorea; reversible; extrapyramidal.

## INTRODUCTION

Valproate (VPA) is an effective anticonvulsive drug with a high tolerability. Its mechanism of action is probably based on selective potentiation of gamma-aminobutyric acid (GABA)-mediated postsynaptic inhibition or on direct GABA increment in the brain[1]. Animal studies have demonstrated that a mono-unsaturated metabolite of VPA, $\delta^2$ valproic acid, accumulates in selected regions of the brain: substantia nigra, superior and inferior colliculus, hippocampus and medulla[2]. Tremor is the most common adverse effect (10%) of VPA on the central nervous system[3]. Infrequent adverse effects of VPA include acute encephalopathy with drowsiness, confusional states[4] and asterixis; choreiform movements occurring within 30 minutes of taking VPA[5]; and sensorineural hearing loss following chronic treatment[6]. In our study, we report a patient with partial and secondarily generalized seizures taking 1500 mg/day VPA. During the second month of the therapy, generalized chorea was observed which was completely reversible after cessation of VPA.

## CASE REPORT

A 38-year-old man was admitted to our clinic with secondarily generalized seizures originating in the temporal lobe. There was no family history of neurological disease. His seizures started 15 years before a traffic accident. He experienced his seizures during sleep and the frequency of his seizures increased with time. Originally he was taking carbamazepine. VPA was added to the therapy. After taking VPA 1500 mg/day for two months (and still taking carbamazepine), the patient complained of involuntary movements. Neurologic examination was completely normal except for visible choreiform movements involving the trunk, head, and upper and lower extremities. Laboratory examination including tests of thyroid function, acute phase reactants, complete blood count, electrolytes and arterial ammonia levels were normal. His blood smear was free of acanthocytes. There were no epileptiform abnormalities on interictal electroencephalography. Cranial magnetic resonance imaging showed no abnormality. The serum VPA level was 40 $\mu$g/dl. Since other aetiologic causes

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of chorea had been excluded, the acute chorea in the patient was thought to be related to VPA usage because of the persistence of choreiform movements, day after day without any fluctuation. VPA was withdrawn and lamotrigine was added eventually at a dose of 400 mg/day. Two months after the cessation of the VPA, choreiform movements had disappeared. The patient has been seizure- and chorea-free since that period.

## DISCUSSION

Transient Parkinsonian symptoms associated with VPA have already been reported in a few studies[2,6]. In these studies, the Parkinsonian symptoms were reduced by levodopa plus carbidopa therapy and disappeared completely two months after discontinuation of VPA. The possible mechanism leading to the appearance of Parkinsonism during VPA treatment is not known, but transient imbalance between functionally reciprocal subgroups of GABA pathways leading to dopamine inhibition has been suggested as part of the aetiology of Parkinsonism induced by VPA[7]. Choreiform movements associated with VPA usage have been described more rarely than Parkinsonian symptoms[5]. Lancman *et al.*[5] presented three patients who developed chorea during long-term treatment with VPA. All the patients had severe brain damage and one had a pre-existing unilateral vascular lesion in the caudate nucleus. The choreic movements involved the head, mouth, tongue, trunk and limbs bilaterally in two cases and contralaterally in the patient with the caudate lesion. Our case had had a head trauma 15 years ago, but his brain magnetic resonance imaging did not reveal any lesion around his basal ganglia. The VPA treatment was added while the patient was using carbamazepine. The similarities between Lancman's[5] patients and our case were the history of brain injury and other antiepileptic drug usage are known, together with VPA. Lancman's patients were taking phenytoin in addition to VPA. Lancman concluded that VPA-induced chorea might be more likely to develop if VPA was taken together with phenytoin. We agree with Lancman[5] that sustained brain injury and any other antiepileptic drug usage seem to be risk factors for VPA-associated chorea. The chorea occurrence did not correlate with VPA overdose in our case since the blood level for VPA was in what is customarily said to be the therapeutic range for VPA.

## CONCLUSION

The mechanism underlying chorea associated with VPA is, as yet, unclear. However, this rare adverse effect of VPA is not a toxic effect and is reversible by cessation of the drug. Patients with head trauma using any other antiepileptic agent together with VPA are at risk of having choreiform movements. Carbamazepine as well as phenytoin increases the risk of the development of VPA-associated choreiform movements when used together with VPA.

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